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论文

MDS、AA和AL患者骨髓细胞周期及增殖特征的研究

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摘要：

目的 检测骨髓增生异常综合征(MDS)、再生障碍性贫血（AA）和急性白血病（AL）患者骨髓单个核细胞（BMMNC）的细胞周期分布及CD34、Ki67抗原的表达。方法 选取2009年6月至2010年6月在山东大学附属省立医院就诊的住院及门诊患者68例，MDS组30例,其中难治性贫血（RA）组18例，难治性贫血伴原始细胞增多(RAEB)组12例；AA组22例,其中急性重型再障组7例，慢性非重型再障组15例；AL组16例，其中急性髓系白血病（AML）组12例，急性淋巴细胞白血病（ALL）组4例。另外选取正常对照组18例（均为非血液病患者）。应用流式细胞仪（FCM），通过碘化丙啶细胞核染色及免疫荧光双标法，对其BMMNC的细胞周期分布及CD34、Ki67的表达进行检测。结果 与正常对照组相比,MDS和AL组BMMNCs中细胞周期G0/G1期、造血干/祖细胞CD34+细胞、Ki67+细胞、CD34+Ki67+细胞、CD34+细胞中Ki67+细胞和Ki67+细胞中CD34+细胞比例均显著升高（P<0.05），而细胞周期S和S+G2/M期细胞比例均显著降低（P<0.05）；AL组细胞周期G2/M期细胞比例亦显著降低（P<0.05）。RAEB组与RA组以及AL组与RAEB组相比，RAEB组和AL组的G0/G1期、CD34+、Ki67+、CD34+Ki67+、CD34+ 细胞中Ki67+ 和Ki67+ 细胞中CD34+ 细胞比例均显著升高（P<0.05），而S、S+G2/M期细胞比例均显著降低（P<0.05）。与正常对照组相比，AA组BMMNC中G0/G1、S、G2/M和S+G2/M期细胞比例的差异均无统计学意义（P>0.05），而其CD34+、CD34+Ki67+ 、CD34+ 细胞中Ki67+和Ki67+细胞中CD34+细胞比例均显著降低（P<0.05）。与AA 组相比，RA组的G0/G1期、CD34+、Ki67+、CD34+Ki67+、CD34+细胞中Ki67+和Ki67+细胞中CD34+细胞比例均显著升高（P<0.05），而S和S+G2/M期细胞比例均显著降低（P<0.05）。结论 本研究表明，AA不同于MDS与AL，MDS和AL具有相似的发病机制，并且BMMNC的细胞周期分布及增殖特性的差异可作为RA与AA的诊断和鉴别诊断指标。

关键词： 骨髓增生异常综合征；贫血，再生障碍性；急性白血病；细胞周期；细胞增殖

Cell cycle distributions and cell proliferation-related protein expression in myelodysplastic syndromes, aplastic anemia, and acute leukemia

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Abstract:

Objective To explore cell cycle distributions and expressions of CD34 and Ki67, and cell proliferation-related proteins in bone marrow mononuclear cells(BMMNCs) among myelodysplastic syndromes(MDS), aplastic anemia(AA), and acute leukemia(AL) patients. Methods Bone marrow aspirates were collected from 68 patients between June 2009 and June 2010 at the Department of Hematology, Provincial Hospital affiliated to Shandong University.The cases consisted of 30 MDS (18 refractory anemia and 12 refractory anemia with excess blasts), 22 AA (7 severe and 15 non-severe cases), and 18 AL (12 acute myeloid leukemia and 4 acute lymphoblastic leukemia). 18 healthy individuals without any hematological problems were used as normal controls. Propidium iodide and immunofluorescent double staining through flow cytometry were applied to explore the cell cycle distributions and expression of CD34 and Ki67. Results Compared with the control group, the percentages of G0/G1 phase of the cell cycle, haemopoietic stem/progenitor cells CD34+ cells, Ki67+ cells, CD34+Ki67+ cells, Ki67+ cells in CD34+ cells, and CD34+ cells in Ki67+ cells of BMMNCs were all significantly increased in the MDS and AL group(P<0.05), whereas the percentages of S and S+G2/M phases of the cell cycle were both significantly decreased(P<0.05). In addition, the proportion of G2/M phase of the cell cycle was lower in the AL group than the control group(P<0.05). The ratios of G0/G1 phase, CD34+ cells, Ki67+ cells, CD34+Ki67+ cells, Ki67+ cells in CD34+ cells, and CD34+ cells in Ki67+ cells were significantly higher in RAEB(refractory anemia with excess blasts) compared to RA (refractory anemia) and in AL compared to RAEB (P<0.05), accompanied by lower ratios of S and S+G2/M phases (P<0.05). There were no significant differences in the ratios of G0/G1, S, G2/M, and S+G2/M phases of BMMNCs between the AA and the control group (P>0.05), whereas the proportions of CD34+, CD34+Ki67+, Ki67+ cells in CD34+ and CD34+ cells in Ki67+ cells were all significantly lowered in the AA group (P<0.05). The percentages of G0/G1 phase, CD34+ cells, Ki67+ cells, CD34+Ki67+ cells, Ki67+ cells in CD34+ cells, and CD34+ cells in Ki67+ cells were more significantly increased in the RA group than in the AA group (P<0.05), whereas the ratios of S and S+G2/M phases were both significantly decreased (P<0.05). Conclusion This study suggests that AA is different from MDS and AL. There is similar pathogenesis for MDS and AL. Analyses of the cell cycle and cell proliferation in bone marrow mononuclear cells are reliable approaches for the diagnosis and differential diagnosis of RA and AA.

Keywords: Myelodysplastic syndromes; Anemia, aplastic; Acute leukemia; Cell cycle; Cell proliferation

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